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Applicant: Bannon, et al.
Serial No.: 09/494,096
Filed: January 28, 2000
For: METHODS AND REAGENTS FOR DECREASING CLINICAL REACTIONS TO ALLERGY

Examiner: Huynh, P.
Art Unit: 1644

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APPEAL BRIEF UNDER 37 C.F.R. § 1.192

Applicant appeals to the Board of Patent Appeals and Interferences (the "Board") from the Examiner's rejection of claims 37-46 and 56-61. A Notice to this effect was filed pursuant to 37 C.F.R. § 1.191(a) on December 5, 2003. The stamped return postcard that was filed with the Notice was received by Applicant indicating that the Notice was received by the Patent and Trademark Office on December 8, 2003.

Filed herewith is a Petition under 37 C.F.R. § 1.136 for a five (5) month extension of time, from February 8, 2004, up to and including July 8, 2004, to file this Appeal Brief (the "Brief"). Pursuant to 37 C.F.R. § 1.192(a), this Brief is being filed in triplicate.

Also enclosed are checks to cover the $1005.00 fee under 37 C.F.R. § 1.17(a)(5) for the Petition and the $165.00 fee under 37 C.F.R. § 1.17(c) for the Appeal Brief. Please charge any additional fees (or credit any overpayment), to our Deposit Account 03-1721.

Real Parties in Interest

As a result of assignments by the inventors, the real parties in interest in this application are the University of Arkansas ("UArk"), SEER Pharmaceuticals LLC (f/k/a Panacea Pharmaceuticals, LLC), and the Mt. Sinai School of Medicine of the City University of New York ("Mt Sinai"). An assignment from inventors Garry Bannon, Wesley Burks, Nina King, Soheila Maleki, Cathie Connaughton, Randall Kopper, Patrick Rabjohn, David Shin and Cesar

Compadre to UArk was recorded in the Patent and Trademark Office on July 17, 2000 at Reel 010972, Frame 0392. An assignment from inventor Howard Sosin to Panacea Pharmaceuticals, LLC was recorded in the Patent and Trademark Office on July 17, 2000 at Reel 010972, Frame 0326. A Certificate of Amendment changing the name of Panacea Pharmaceuticals, LLC to SEER Pharmaceuticals, LLC was filed with the Secretary of State of the State of Delaware on October 25, 2002. A copy of this Certificate was filed for recordation with the Patent and Trademark Office on October 16, 2003. An assignment from inventor Hugh Sampson to Mt Sinai was recorded in the Patent and Trademark Office on July 17, 2000 at Reel 010972, Frame 0339.

Related Appeals and Interferences

Appellant has filed Appeal Briefs for co-pending applications U.S. Serial No. 09/455,294 (Original Brief filed October 10, 2003 and Amended Brief filed June 1, 2004); U.S. Serial No. 09/478,668 (Original Brief filed June 12, 2003 and Amended Brief filed March 23, 2004); and U.S. Serial No. 09/731,375 (Original Brief filed October 10, 2003 and Amended Brief filed June 1, 2004) addressing some issues that overlap with the issues presented here. Appellant also expects to file an Appeal Brief for co-pending application U.S. Serial Nos. 09/141,220 addressing some issues that overlap with the issues presented here. No other pending appeals or interferences are known to Appellant, Appellant's legal representative, or Appellant's assignee that will directly affect or be directly affected by the Board's decision in this appeal. Similarly, no other pending appeals or interferences are known that may have a bearing on the Board's decision in this appeal.

Status of Claims

The application was filed with claims 1-36. Claims 1-36 were the subject of a Restriction Requirement mailed March 21, 2001. Claims 1-29 and 33-36 were withdrawn July 20, 2001 in response to the Restriction Requirement. Claims 30-32 were examined in an Office Action mailed March 12, 2002. Claims 1-36 were canceled in an Amendment filed September 12, 2002; claims 37-67 were added. Claims 37-67 were finally rejected in an Office Action mailed July 30, 2003. A Request to withdraw the finality of the Office Action was submitted August 26, 2003. The Request was rejected in an Advisory Action mailed September 29, 2003. A Notice

appealing the rejection of claims 37-67 was filed December 5, 2003. An Amendment canceling claims 47-55 and 62-67 was filed with the Notice. An Advisory Action was mailed January 2, 2004 indicating that the Amendment had been entered. Thus, claims 37-46 and 56-61 are pending and stand rejected. The rejection of claims 37-46 and 56-61 is hereby appealed. A listing of pending claims 37-46 and 56-61 is provided as **Attachment I**.

Status of Amendments

This Brief is being submitted together with an Amendment that amends claim 42 to correct an error in antecedent basis that was highlighted by the Examiner under § **8** of the Final Office Action mailed July 30, 2003. A copy of claims 37-46 and 56-61 that will be pending after entrance of the Amendment is provided as **Attachment II**. For the purpose of this Brief, Appellant is assuming that the Amendment will be entered since the minor amendments to claim 42 reduce the number of issues under appeal. Accordingly, in the following the issues on appeal will be discussed as if they applied to the claims that will be pending *after* entrance of the Amendment.

Summary of Invention

Generally, the present invention is directed to nucleotide molecules that encode modified protein allergens. The claims on appeal are limited to nucleotide molecules that encode modified *food* allergens. The modified food allergens have amino acid sequences that are substantially identical to those of corresponding unmodified food allergens except that at least one amino acid has been modified in at least one IgE epitope. The modified food allergens have a reduced ability to bind IgE antibodies and are useful in treating food allergies.

The present specification includes data and working examples demonstrating the identification and modification of IgE epitopes in the peanut allergens Ara h 1, Ara h 2 and Ara h 3 (see Examples 1-2 and 4). Peanut allergens are the most potent known protein allergens. *In vitro* (see Examples 3 and 5) and *in vivo* (see Example 7) experiments that were performed with a modified Ara h 2 protein are also discussed. The specification also describes other known food allergens that can be modified according to the teachings of the invention (e.g., allergens from milk, grains, soybeans, eggs, fish, crustaceans, mollusks, etc.). The specification further provides references that describe known IgE epitopes for a number of these food allergens.

Issues

The issues on appeal are (referring to §§ **4-15** of the Final Office Action mailed July 30, 2003):

(1) Are claims 37-46 and 56-61 invalid for lack of enablement (see § **4**)?

(2) Are claims 37-46 and 56-61 invalid for lack of written description (see § **5**)? Specifically, can the written description requirement ever be satisfied for claims relating to nucleotide molecules without an explicit recitation in the specification of every sequence encompassed by the claims?

(3) Are claims 37 and 56-60 invalid for containing new matter (see § **6**)? Appellant notes that claim 37 does not include the language that the Examiner objects to under this rejection. Thus the rejection presumably only applies to claims 56-60.

(4) Are claims 41-42 indefinite (see § **8**)? Appellant notes that claim 41 does not include the language that the Examiner objects to under this rejection. Thus the rejection presumably only applies to claim 42.

(5) Are claims 37-45 and 56-61 obvious in light of Burks et al. (1997) and Evens et al. (1993) (see § **12**)? Specifically, is a reference available as prior art to a continuation-in-part application when (a) the entire contents of the reference were included in a priority application that was filed before publication of the reference and (b) the entire contents of the reference were also included in the continuation-in-part application and all intervening applications?

(6) Are claims 37-46 and 56-61 obvious in light of Stanley et al. (1997) and Evens et al. (1993) (see § **13**)? Specifically, is a reference available as prior art to a continuation-in-part application when (a) the entire contents of the reference were included in a priority application that was filed before publication of the reference and (b) the entire contents of the reference were also included in the continuation-in-part application and all intervening applications?

(7) Are claims 37-45 and 56-61 unpatentable over claims 1-4 and 7 of U.S. Pat. No. 6,486,311 under the judicially created doctrine of obviousness-type double patenting (see § **15**)?

Grouping of Claims

The claims stand or fall together for issues numbered (1)-(7) above, as indicated below:

(1) Claims 37-46 and 56-61 stand or fall together.

(2) Claims 37-46 and 56-61 stand or fall together.

(3) Claim 37 stands or falls alone; claims 56-60 stand or fall together.

(4) Claims 41-42 stand or fall separately.

(5) Claims 37-45 and 56-61 stand or fall together.

(6) Claims 37-46 and 56-61 stand or fall together.

(7) Claims 37-45 and 56-61 stand or fall together.

Argument

ISSUE 1: Claims 37-46 and 56-61 are not invalid for lack of enablement

Claims 37-46 and 56-61 stand rejected for lack of enablement. With respect to this rejection all claims stand or fall together. In supporting this rejection, the Examiner cites *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) and states that the disclosure in the specification is insufficient to enable one skilled in the art to practice the broader claimed invention without an undue amount of experimentation. This rejection is respectfully traversed; reconsideration and withdrawal is requested.

As acknowledged by the Examiner, the present application provides explicit exemplification of nucleotide molecules encoding suitably modified peanut allergens and methods of preparing them. The disputed enablement issue in this case is whether, in light of the teachings of the specification, undue experimentation is required to obtain modified food allergens *other than* those that are specifically exemplified in the specification. In this context, Appellant and the Examiner agree that *Wands* is the relevant precedent. The question, therefore, is whether the experimentation required to obtain the broader claimed nucleotide molecules would be more burdensome or complex, or less likely to result in success, than the experimentation required in *Wands*. If not, the inventors are entitled to allowance of the disputed claims. The answer to this question is obtained by comparison of the experimental procedures in the two cases. We begin by summarizing *Wands*.

In re Wands

In *Wands*, the inventors developed a diagnostic for the Hepatitis B virus. In particular, the inventors identified a particular antibody that bound to a viral protein and could, therefore, be used to determine whether the virus was present. In *Wands*, the claims were broad enough to encompass both the particular antibodies described in the specification and other antibodies

having the same or similar characteristics. The broadest claim encompassed any monoclonal, high affinity IgM antibody "having a binding affinity constant [...] of at least 10^9 M^{-1}." The specification described work by the inventors that led to the production of four antibodies falling within the scope of the claim. One hybridoma (a cell fusion that produces a single antibody) was deposited with the ATCC. Thus, the specification exemplified, at most, four antibodies that fell within the claim. The claim, however, encompassed all antibodies having the recited characteristics – a potentially infinite number of antibodies.

The Examiner rejected the Wands claim as too broad. He said that the disclosure in the specification was not commensurate in scope with the claim, that "the production of high Affinity IgM [...] antibodies is unpredictable and unreliable, so that it would require undue experimentation for one skilled in the art to make the antibodies." *Id.* at 735.

The Federal Circuit reversed the Examiner (and the Board of Appeals). The Court held that the identification and production of other embodiments of the invention could have been achieved without undue experimentation. The Court said that "[a] patent need not disclose that which is well known in the art." *Id.* at 735. The Court held that the generic claims should have been allowed because (1) the starting materials necessary to obtain the generically described (i.e., non-exemplified) antibodies were available to the public, (2) the methods used to generate antibodies and to screen them to determine which fall within the claims were well known in the art, and (3) useful antibodies could therefore be obtained without undue experimentation.

The case turned on the concept of undue experimentation. The Court said that a "considerable amount of experimentation is permissible, if it is merely routine." *Id.* at 737. The Court then described the experimental procedure that would have been followed by scientists attempting to produce antibodies that were not expressly described in the *Wands* specification but that fell within the generic claims of the *Wands* application:

1. "The first step [...] is to immunize an animal." (p. 737)
2. "Next the [mouse's] spleen [...] is removed and the lymphocytes [in the spleen] are separated from the other spleen cells." (p. 737)
3. "The lymphocytes are mixed with myeloma cells, and the mixture is treated to cause a few of the cells to fuse with each other, thus creating hybridomas." (p. 737)

4. "Hybridoma cells that secrete the desired antibodies then must be isolated from the enormous number of other cells in the mixture. This is done through a series of screening procedures [of which] the first step is to separate the hybridoma cells from unfused lymphocytes and myeloma cells." (p. 737)

5. "The next step [of the screening procedures] is to isolate and clone hybridomas that make antibodies that bind to the antigen of interest. Single hybridoma cells are placed in separate chambers and are allowed to grow and divide." (p. 737)

6. "After there are enough cells in the clone to produce sufficient quantities of antibody to analyze, the antibody is assayed to determine whether it binds to the antigen." (pp. 737-738)

7. Antibodies that fall within the claims are selected by determination of their "numerical affinity constant, which must be measured using the [...] laborious Scotchard analysis." (p. 738)

8. There is then performed "further screening to select those [antibodies] which have an IgM isotype and have a binding affinity constant of at least 10^9 M^{-1}." (p. 738)

The *Wands* inventors used these techniques. Some fusions were unsuccessful and produced no hybridomas; others produced hybridomas that made antibodies to the Hepatitis B surface antigen. Certain of these antibodies were screened. Some of the screened antibodies fell within the claims; others did not.

No undue experimentation in *Wands*

Despite the fact that a substantial amount of experimentation was required in *Wands* to obtain antibodies which were within the scope of the claims, the Court concluded that the experimentation was not "undue" and that the generic claims of the Wands patent were adequately enabled. The Court found that "there was a high level of skill in the art [...] and all of the methods needed to practice the invention were well-known." *Id.* at 740. The Court also found that, although the technology involved screening hybridomas to determine which, if any, secreted antibodies with the desired characteristics, "[p]ractitioners of the art [were] prepared to screen negative hybridomas in order to find one that makes the desired antibody." *Id.* at 740. The Court did not quantify the required likelihood of success, but noted that even a success rate as low as 2.8% would not necessarily require a conclusion of undue experimentation. *Id.* at 740.

This case is similar to *Wands*

As mentioned earlier, and as acknowledged by the Examiner, the present application provides explicit exemplification of nucleotide molecules that encode modified peanut allergens that fall within the scope of claims. The present application clearly states that its teachings are also applicable to other food allergens (e.g., see pages 7-9). The present application clearly sets forth all the steps necessary to identify and prepare suitable nucleotide molecules encoding modified food allergens that fall within the scope of claim 37, namely:

1. Identifying a food allergen whose sequence is to be modified – the sequences of numerous food allergens were known at the time of filing, a number of these are highlighted in the specification, e.g., see pages 7-9; others were known as evidenced by the numerous references and accession numbers that are provided in the "Official list of allergens," maintained by the IUIS Allergen Nomenclature Subcommittee and provided as **Attachment III**.

2. Identifying and modifying IgE binding sites within the food allergen – IgE binding sites were known for a number of food allergens including allergens from milk, egg, codfish, hazel nut, soybean and shrimp (see references cited on page 7); in addition, methods of identifying and modifying IgE binding sites were known and further described in the specification (e.g., see Examples 1 and 2).

3. Introducing mutations into the sequence of nucleotide molecules encoding the food allergen – methods for producing recombinant allergens and for performing site-directed mutagenesis were well known and routine at the time of filing (e.g., see page 11 and Example 3).

4. Screening mutants for those with reduced IgE binding as the natural food allergen (and optionally substantially the same T-cell activity and/or IgG binding) – those skilled in the art were familiar with the methods that were used by the inventors to screen modified protein allergens for IgG and IgE binding and T-cell stimulation (e.g., see page 9 and the Examples).

Thus, as in *Wands*, at the time the application was filed, the starting materials necessary to obtain nucleotide molecules encoding modified protein allergens were available and the techniques for performing the necessary steps were well known and routine. In addition, as was the case in *Wands*, there was a high level of skill in the art. Appellant respectfully submits that now that the inventors have demonstrated that the inventive methods *can* successfully be applied to protein allergens (i.e., that it is possible to generate nucleotide molecules encoding modified

protein allergens to which IgE binding is reduced), those skilled in the art would instantly realize that modified protein allergens derived from other allergens (1) would exist, (2) would operate in the same way to produce the same or similar results and (3) that nucleotide molecules encoding these could be obtained using the techniques described in the application or which were well-known (indeed, routine) in the art.

There is no particular magic in the sequence of the peanut allergens Ara h 1, 2, and 3 that makes these protein allergens more susceptible to the inventive methods; the inventive principles, as discussed in the present application, apply to other protein allergens as well. In fact, quite the opposite might be expected. Peanut proteins are highly allergenic and, like many other food allergens (as distinguished, for example from most pollens and danders) present a significant risk of anaphylaxis to those allergic to them. The inventive demonstration that such anaphylactic proteins can be modified so that IgE binding is reduced as compared with the unmodified protein provides a strong teaching to those of ordinary skill in the art that other modified protein allergens with reduced IgE binding can also be made.

Others have prepared modified protein allergens according to the teachings of the application without undue experimentation

As further evidence that the claimed nucleotide molecules may be obtained without undue experimentation, Appellant has identified a series of references showing that, after the present invention was made, people of ordinary skill in the art followed the steps taught in the present application (i.e., used patient sera to identify IgE binding epitopes, modified the protein sequence to alter identified IgE binding epitopes; and screened modified proteins to identify those with reduced binding) and were able to obtain, without undue experimentation, a variety of nucleotide molecules encoding modified food allergens that lie within the scope of the pending claims. More specifically, the following post-art references (already made of record in the Supplemental Response to Office Action that was filed September 12, 2002) were identified:

A. English walnut allergen

Robotham et al., "Linear IgE epitope mapping of the English walnut (*Juglans regia*) major food allergen, Jug r 1", *J. Allergy Clin. Immunol.* 109:143-149, 2002.

B. Potato allergen

Astwood et al., "Identification and characterization of IgE binding epitopes of patatin, a major food allergen of potato", *J. Allergy Clin. Immunol.* 105:S184 (Abstract 555), 2000.

C. Soybean allergen

Helm et al., "Mutational analysis of the IgE-binding epitopes of P34/Gly m Bd 30K", *J. Allergy Clin. Immunol.* 105:378-384, 2000.

D. Shrimp allergen

Ayuso et al., "Identification and mutational analysis of major epitopes of the shrimp allergen Pen a 1 (Tropomyosin)", *J. Allergy Clin. Immunol.* 105:S140 (Abstract 423), 2000.

Lehrer et al., "Current understanding of food allergens", *Ann. N.Y. Acad. Sci.* 964:69-85, 2002.

Appellant respectfully submits that this evidence reinforces the fact that there is no particular magic in the sequence of peanut allergens that makes these allergens more susceptible to mutation; the inventive principles, once demonstrated may be readily applied to other protein allergens, including food allergens.

The Examiner's arguments fail to establish a case for lack of enablement

The Examiner begins the rejection by laboriously listing twelve different embodiments that she concedes **are** enabled by the specification (see pages 2-3 of the Office Action mailed July 30, 2003). In essence the Examiner states that the specification is *only* enabling for nucleotide molecules that encode the specific modified *peanut* allergens whose *sequences* are explicitly listed in the specification. The absurdity of the Examiner's position is readily appreciated by considering one of these limited embodiments. For example, under embodiment (2) on page 2 of the Office Action, the Examiner states that the application is only enabling for a *single* Ara h 2 nucleotide, namely a nucleotide that encodes:

> "a modified peanut allergen whose amino acid sequence is substantially identical to that of an unmodified peanut allergen of SEQ ID NO:4 [i.e., wild-type Ara h 2] except that at least one amino acid has been substituted in at least one IgE epitope wherein the amino acids at position 20, 31, 60 and 67 has [sic] been substituted for alanine".

This embodiment corresponds to the modified Ara h 2 protein of Examples 3, 5 and 7. The Examiner is essentially taking the position that the specification does not enable *any* variations

from this specifically modified Ara h 2 protein. Under this logic, a skilled person, having read the present application would be incapable of preparing (without undue experimentation) a nucleotide molecule encoding a modified Ara h 2 with a different substitution (e.g., methionine instead of alanine) and/or a mutation at one of the others sites identified in Table 5. This position is just silly. The proper legal question is not "did Appellant *reduce to practice* and *explicitly recite* every nucleotide molecule encoding a modified peanut allergen that falls within the scope of the claims?" Instead, the question is "would a skilled person be capable of producing nucleotide molecules encoding modified peanut allergens that fall within the scope of the claims without undue experimentation?"

The present specification sets forth the complete amino acid sequence of Ara h 2 (SEQ ID NO. 2), and also the nucleotide sequences of gene that encodes it (SEQ ID NO. 3). The specification further sets out the amino acid sequences of each of 10 IgE epitopes mapped in the Ara h 2 protein (Table 2). The specification further describes particular alanine or methionine substitutions that were introduced into the mapped IgE binding sites, and shows that some of these substitutions result in decreased IgE binding (Table 5). In discussing these data, the specification states (see page 25, lines 11-23):

> "The results discussed above for Ara h 1, Ara h 2, and Ara h 3 demonstrate that once an IgE binding site has been identified, it is possible to reduce IgE binding to this site by altering a single amino acid of the epitope. [...] Besides finding that many epitopes contained more than one residue critical for IgE binding, it was also determined that more than one residue type (ala or met) could be substituted at certain positions in an epitope with similar results. This allows for the design of a hypoallergenic protein that would be effective at blunting allergic reactions for a population of peanut sensitive individuals."

Thus, the specification specifically highlights that substitutions at different positions, and with different amino acids, achieved the same results.

The Examiner is correct that Appellant did not reduce to practice each and every possible disruption to Ara h 2 IgE sites. However, a skilled person, reading the specification, would understand, indeed would explicitly be told, that the presented substitutions were merely exemplary and others would work as well. A skilled artisan would appreciate that the techniques described in the specification would successfully identify all such substitutions without undue

experimentation. That is, a skilled person would understand that the inventors had enabled the invention to the full scope of claim 47.

A claim limited to the particular substitutions that the inventors happened to have made prior to filing their patent application is virtually useless. Anybody of ordinary skill in the art could prepare a nucleotide molecule encoding a modified peanut allergen that falls outside the scope of such a claim but still embodies the spirit, scope, and teachings of Appellant's contribution. If the legal standard of enablement in fact required reduction to practice of every possible useful sequence, as asserted by the Examiner, patent applicants would be forced to perform useless and wasteful experiments (potentially endlessly) merely to ensure that they could protect their contributions. Such a standard would eviscerate the patent system.

The Examiner also cites various references that include a discussion of mutated peptides that failed to exhibit reduced IgE binding (Burks et al. and Stanley et al.) or T-cell stimulation (Fasler et al.) as compared to wild-type peptides (see pages 8-9 of the Office Action mailed July 30, 2003). The Examiner suggests that these failures highlight the lack of predictability in the preparation of a nucleotide molecule that would encode a suitably modified protein allergen. However, the Examiner fails to recognize that even though the possibility exists that the initial modification of IgE binding epitopes may *not* identify suitable modified proteins, as was the case in *Wands* (and also in Burks et al., Stanley et al. and Fasler et al.), practitioners would be prepared to test more than one modification and to screen for nucleotide molecules that encode useful modified proteins. The present case need only meet the enablement standard that was set in *Wands*. Appellant respectfully submits that the standard has been met, reconsideration and withdrawal of the rejection for lack of enablement is therefore requested.

ISSUE 2: Claims 37-46 and 56-61 are not invalid for lack of written description

Claims 37-46 and 56-61 stand rejected for lack of written description. With respect to this rejection all claims stand or fall together.

The written description requirement imposes a duty on patent applicants to notify the public of the scope and content of their inventions. The requirement is satisfied if one skilled in the art would reasonably conclude that the inventors were in possession of the claimed invention at the time the patent application was filed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991). Furthermore, there is a strong presumption that claims submitted with an application

are adequately described by the application. *In re Wertheim* 541 F.2d 257 (Fed. Cir. 1993). Claim 37 was present in substantially the same form as claim 30 in the application as originally filed – it has simply been limited to food allergens as described on page 8 of the original specification. Claims 38-42 recite the specific modifications that are described on page 4, lines 17-23 and the Examples. Claim 43 recites the properties described on page 4, lines 8-14 and 26-28. Claim 44 recites the limitations found on page 12 and Example 3. Likewise, claims 45-46 simply recite relevant subsets of food allergens that were described on pages 7-9 and the Examples of the specification as filed. Finally, claims 56-61 recite the limitations found in original claim 30 and the data of Table 6 of the specification as filed (see discussion under Issue 3 below). The burden is therefore on the Examiner to overcome the strong presumption of descriptive support with evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims. The Examiner has not, and cannot meet this burden; the claimed invention is appropriately described in the specification.

Both in her written rejections and in an in-person interview, the Examiner has indicated that, in her view, the written description requirement (like the enablement requirement) can never be satisfied for a nucleic acid or protein unless the complete sequence is explicitly set forth in the specification and recited in the claim by way of a SEQ ID NO. The same Examiner is responsible for the prosecution of a large number of related cases; we are unable to move prosecution forward without first resolving the question of whether the written description requirement can ever be satisfied without recitation of a SEQ ID NO. in the claim.

According to the Examiner the written description requirement is not satisfied in this case for *any* nucleotide molecules other than those encoding peanut allergens that have been modified by substitution with *alanine* or *methionine* at those *specific locations* listed in Tables 4, 5 and 6 (see pages 10-11 of Office Action mailed July 30, 2003). This is clearly not the law nor should it be. The proper legal question for a written description analysis is "would a skilled person recognize that Appellant was in *possession* of the nucleotide molecules encoding modified peanut allergens that fall within the scope of the claims?"

As discussed above, the present specification sets forth the complete amino acid sequences of Ara h 1, 2, and 3 (SEQ ID NOs. 2, 4 and 6), and also the nucleotide sequences of genes that encode them (SEQ ID NOs. 1, 3 and 5). The specification further sets out the amino

acid sequences of each of 23 IgE epitopes mapped in the Ara h 1 protein (Table 1), the amino acid sequence of each of 10 IgE epitopes mapped in the Ara h 2 protein (Table 2), and the amino acid sequence of each of 4 epitopes mapped in the Ara h 3 protein (Table 3). The specification further describes particular alanine or methionine substitutions that were introduced into the mapped IgE binding sites, and shows that some of these substitutions result in decreased IgE binding (Tables 4-6). In discussing these data, the specification states (see page 25, lines 11-23):

> "The results discussed above for Ara h 1, Ara h 2, and Ara h 3 demonstrate that once an IgE binding site has been identified, it is possible to reduce IgE binding to this site by altering a single amino acid of the epitope. [...] Besides finding that many epitopes contained more than one residue critical for IgE binding, it was also determined that more than one residue type (ala or met) could be substituted at certain positions in an epitope with similar results. This allows for the design of a hypoallergenic protein that would be effective at blunting allergic reactions for a population of peanut sensitive individuals."

Thus, the specification specifically highlights that substitutions at different positions, and with different amino acids, achieved the same results.

Appellant has already conceded that the Examiner is correct that the specification does not explicitly set forth the sequences of all possible disruptions to Ara h 1, Ara h 2, and Ara h 3 IgE sites. However, a skilled person, reading the specification, would understand, indeed would explicitly be told, that the presented substitutions were merely exemplary and others would work as well. A skilled artisan would appreciate that the techniques described in the specification would successfully identify all such substitutions. That is, a skilled person would understand that the inventors were in *possession* of the invention to the full scope of the claims.

Appellant reiterates that a claim limited to the particular substitutions that the inventors happened to have made prior to filing their patent application is virtually useless. Anybody of ordinary skill in the art could prepare a nucleotide molecule encoding a modified peanut allergen that falls outside the scope of such a claim but still embodies the spirit, scope, and teachings of Appellant's contribution. If the legal standard of written description in fact required verbatim recitation of every possible useful sequence, as asserted by the Examiner, patent applicants would be forced to perform useless and wasteful experiments (potentially endlessly) merely to ensure that they could protect their contributions, or alternatively would be motivated to include

endless lists of sequences in their patent applications merely to ensure that all contemplated embodiments are "described". Such a result would have no beneficial purpose.

Claim 37, the only independent claim in the application recites:

> "A nucleotide molecule encoding a modified food allergen whose amino acid sequence is substantially identical to that of an unmodified food allergen except that at least one amino acid has been modified in at least one IgE epitope so that IgE binding to the modified food allergen is reduced as compared with IgE binding to the unmodified food allergen, the at least one IgE epitope being one that is recognized when the unmodified food allergen is contacted with serum IgE from an individual that is allergic to the unmodified food allergen."

The specification explicitly sets out the sequence of several examples of nucleotide molecules that encode modified peanut allergens. These modified peanut allergens are described as "exemplary" of the inventive principles. For example, the specification recites that "Peanut allergens (Ara h 1, Ara h 2, and Ara h 3) have been used in the examples to demonstrate alteration of IgE binding sites while retaining binding to IgG and activation of T cells" (page 4, lines 15-17). The specification also points to several other common food allergens (see page 8, lines 1-3: "Examples of common food allergens include proteins from peanuts, milk, grains such as wheat and barley, soybeans, eggs, fish, crustaceans, and mollusks."). Moreover, the specification provides references for food allergens *whose IgE epitopes had already been* identified (see page 8, lines 4-13). The specification also describes techniques for modifying sequences within IgE sites (see, for example, page 10, lines 3-6 and Examples 2-3), and for identifying those modifications that reduce IgE binding (see, for example, page 4, lines 24-28 and Examples 1-2) in accordance with claim 37.

And, of course, the specification provides evidence that the inventive strategy successfully produced modified peanut allergens with reduced IgE reactivity and thus nucleotide molecules encoding these. The teachings and guidance provided by this success are far-reaching. As discussed above and in the specification, peanut allergy is one of the most potent allergies. Indeed, as noted in the specification (see page 16, lines 4-11):

> "Peanut allergy is one of the most common and serious of the immediate hypersensitivity reactions to foods in terms of persistence and severity of reaction. [...] The majority of cases of fatal food-induced anaphylaxis involve ingestion of peanuts [...]."

A person of ordinary skill in the art would immediately understand the exciting implications of the inventive exemplification of reduced-allergenicity peanut allergens: if it works for peanuts, it will work for other food allergens.

The claimed nucleotide molecules all encode proteins; sensitized individuals are all exposed to food allergens by the same route (i.e., ingestion); food allergens are all readily modified according to the same techniques, and those with reduced allergenicity are identified in the same manner. Reading the present specification, those of ordinary skill in the art will immediately appreciate that modified food allergens with reduced allergenicity, according to the present claims, exist, and can readily be made according to the teachings of the specification. In other words, those of ordinary skill in the art will immediately appreciate that the inventors were *in possession of* the claimed invention. Denial of claims to nucleotide molecules encoding modified food allergens would deprive the present inventors of protection commensurate in scope with their contribution, and would create silly incentives disruptive to science, the patent process, and commerce.

Appellant appreciates that certain court decisions, including *University of California v. Eli Lilly and Co.* have been interpreted to stand for the proposition that, in certain cases, nucleic acid or protein molecules cannot be properly described in a patent specification without explicit recitation of sequence information. However, this is not such a case. First, significant sequence information *is* provided for this case. Furthermore, a determination of whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by those skilled in the art *at the time that the invention was filed* (*In re Alton*, 76 F3d 1168, 37 USPQ 2d 1578 (Fed. Cir. 1996)). In *University of California v. Eli Lilly and Co.*, the patent applications in issue were filed in 1977 and 1979; the present application was filed 20 years later. A lot happened in the intervening 20 years. Automated sequencing and synthesis technologies were developed; PCR was invented; a variety of techniques for disrupting or otherwise mutagenizing a nucleic acid sequence were standardized. Mechanical application of a "Sequence Listing or bust" rule vitiates the very purpose of the *Lily* ruling, which was to ensure that the scope of patent claims was commensurate in scope with the contribution. The present specification describes the invention of nucleotide molecules encoded modified protein allergens for a wide variety of food allergens; the pending claims are of appropriate scope. For all of these

reasons, the Examiner's rejection of the pending claims for lack of written description, should be removed.

ISSUE 3: Claims 37 and 56-60 are not invalid for containing new matter

The Examiner has questioned the support for the recitation in claims 56-60 of a nucleotide molecule encoding a modified protein allergen that comprises at least one IgE epitope with 1-6, 1-5, 1-4, 1-3 or 1-2 modified amino acid residues. The Examiner included claim 37 under this rejection; however, claim 37 does not include the language that the Examiner objects to. Thus, with respect to this rejection claim 37 stands or falls alone and claims 59-60 stand or fall together.

Appellant respectfully submits that these claims are fully supported by the specification and claims as originally filed. In particular, original claim 30 reads "A nucleotide molecule encoding a modified allergen [...] comprising at least one IgE binding site [...] modified by *at least one* amino acid change [...]." Original claim 30 therefore makes it perfectly clear that the present invention encompasses nucleotide molecules encoding modified protein allergens with at least one IgE binding site that includes *more than one* modified amino acid residue. The specification as filed further teaches IgE epitopes that include 1, 2, 3, 4, 5 or 6 amino acid residues that, when altered, lead to a reduction in IgE binding (e.g., see epitopes 5, 7, 8, 9, 18 in Table 4 and epitope 4 in Table 6, respectively). The specification and claims as originally filed therefore clearly support the language of pending claims 56-60.

ISSUE 4: Claims 41 and 42 are not indefinite

The Examiner has taken the position that claims 41-42 are indefinite under 35 U.S.C. § 112, second paragraph for reciting the limitation "at least one hydrophobic amino acid" without providing antecedent basis in base claim 41. The Examiner included claim 41 under this rejection; however, claim 41 is the base claim and does not include the language that the Examiner objects to. Thus, with respect to this rejection claims 41 and 42 fall or stand separately. As amended herein (see Amendment filed herewith), claim 42 reads "wherein at least one amino acid in the at least one IgE epitope of the unmodified food allergen is hydrophobic, and wherein said at least one hydrophobic amino acid has been substituted by a neutral or hydrophilic amino acid". Appellant respectfully submits that the limitations of claim

42 now have proper antecedent basis and that claim 42 is definite. Withdrawal of the rejection is earnestly requested.

ISSUE 5: Claims 37-45 and 56-61 are not obvious in light of Burks et al. (1997) and Evens et al. (1993)

The Examiner has rejected claims 37-45 and 56-61 as being unpatentable under 35 U.S.C. § 103(a) in light of Burks et al. (*Eur. J. Biochem.* 245:334-339, 1997) and Evens et al. (*Therapeutic Drug Monitoring* 15: 514-520, 1993). With respect to this rejection all claims stand or fall together.

This rejection should be removed quite simply because Burks (1997) is not prior art. The relevant teachings of Burks (1997) were included near *verbatim* in priority documents U.S. Serial No. 08/717,933 filed September 23, 1996 (see pp. 135-155, 175, and 178-180, the "1996 filing") and U.S. Serial No. 09/141,220 filed August 27, 1998 (see pp. 7-11 and 16-29, the "1998 filing"). The 1996 filing was made by Appellant in part to protect the teachings of Burks (1997). The present continuation-in-part application properly claims priority to the 1996 filing via the 1998 filing. The teachings of Burks (1997) were again included in the present application (see pp. 7-11 and 16-26). Burks (1997) was published after the 1996 priority date and cannot therefore be used as prior art under 35 U.S.C. § 103(a). Evens (1993) is cited as a secondary reference that teaches certain limitations found only in dependent claims. Accordingly, Evens (1993) alone cannot render obvious claims 37-45 and 56-61. Withdrawal of the rejection is earnestly requested.

ISSUE 6: Claims 37-46 and 56-61 are not obvious in light of Stanley et al. (1997) and Evens et al. (1993)

The Examiner has rejected claims 37-46 and 56-61 as being unpatentable under 35 U.S.C. § 103(a) in light of Stanley et al. (*Archives of Biochemistry and Biophysics* 342(2):244-253, June 1997) and Evens et al. (*Therapeutic Drug Monitoring* 15: 514-520, 1993). With respect to this rejection all claims stand or fall together.

This rejection should also be removed quite simply because Stanley (1997) is not prior art. The relevant teachings of Stanley (1997) were included near *verbatim* in priority documents U.S. Serial No. 08/717,933 filed September 23, 1996 (see pp. 156-174 and 176-180, the "1996

filing") and U.S. Serial No. 09/141,220 filed August 27, 1998 (see pp. 7-11 and 16-29, the "1998 filing"). The 1996 filing was made by Appellant in part to protect the teachings of Stanley (1997). The present continuation-in-part application properly claims priority to the 1996 filing via the 1998 filing. The teachings of Stanley (1997) were again included in the present application (see pp. 7-11 and 16-26). Stanley (1997) was published after the 1996 priority date and cannot therefore be used as prior art under 35 U.S.C. § 103(a). Evens (1993) is cited as a secondary reference that teaches certain limitations found only in dependent claims. Accordingly, Evens (1993) alone cannot render obvious claims 37-46 and 56-61. Withdrawal of the rejection is earnestly requested.

ISSUE 7: Claims 37-45 and 56-61 are not unpatentable over claims 1-4 and 7 of U.S. Pat. No. 6,486,311 under the judicially created doctrine of obviousness-type double patenting

The Examiner has rejected claims 37-45 and 56-61 as being unpatentable over claims 1-4 and 7 of U.S. Pat. No. 6,486,311 under the judicially created doctrine of obviousness-type double patenting. With respect to this rejection all claims stand or fall together.

This rejection should be removed. Claims 1-4 of U.S. Pat. No. 6,486,311 are drawn to a nucleotide molecule that encodes Ara h 2. Claim 7 is to a nucleotide molecule that encodes an Ara h 2 with one or more mutated IgE epitopes. In contrast, the present claims are to a nucleotide molecule that encodes a modified food allergen. The claims are of different scope, and are not obvious over one another. For example, the pending claims encompass nucleotide molecules that encode modified allergens from milks, grains, fish crustaceans and mollusks (see claim 45). These nucleotide molecules are outside the scope of the patent claims and are not obvious over those claims. As another example, the pending claims encompass nucleotide molecules encoding modified allergens that retain the ability to stimulate T-cells (see claim 43). This novel limitation is taught in the present case (e.g., see Example 5) and is not obvious over the patent claims. Conversely, the patent claims are limited to Ara h 2. Appellant respectfully submits that Ara h 2 claims are non-obvious over the pending food claims because they represent a non-obvious species of the claimed genus. Indeed, as discussed above and in the specification, peanut allergens such as Ara h 2 are one of the most potent of allergens. As noted in the specification (see page 16, lines 4-11):

> "Peanut allergy is one of the most common and serious of the immediate hypersensitivity reactions to foods in terms of persistence and severity of reaction. [...] The majority of cases of fatal food-induced anaphylaxis involve ingestion of peanuts [...]."

Thus, based solely on the present modified allergen claims, a skilled person would have lacked the reasonable expectation of success that is necessary to render obvious the modified Ara h 2 species claims. Appellant therefore respectfully submits that a skilled person would recognize that a generic claim to modified food allergens cannot render obvious a claim that is limited to modified Ara h 2.

Conclusion

Appellant again concludes with the belief that claims 37-46 and 56-61 are fully supported by the specification as filed and allowable over the art of record. Allowance of these claims is earnestly requested.

Respectfully submitted,

Dated: July 8, 2004

Charles E. Lyon, D.Phil.
Limited Recognition Under 37 C.F.R. § 10.9(b)

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Attachment I

to

Appeal Brief under 37 C.F.R. § 1.192

Pending Claims before Entrance of Amendment

Pending Claims before Entrance of Amendment

1-36. **(Canceled)**

37. **(Previously presented)** A nucleotide molecule encoding a modified food allergen whose amino acid sequence is substantially identical to that of an unmodified food allergen except that at least one amino acid has been modified in at least one IgE epitope so that IgE binding to the modified food allergen is reduced as compared with IgE binding to the unmodified food allergen, the at least one IgE epitope being one that is recognized when the unmodified food allergen is contacted with serum IgE from an individual that is allergic to the unmodified food allergen.

38. **(Previously presented)** The nucleotide molecule of claim 37 wherein at least one amino acid has been modified in all the IgE epitopes of the unmodified food allergen.

39. **(Previously presented)** The nucleotide molecule of claim 37 wherein the at least one IgE epitope is one that is recognized when the unmodified food allergen is contacted with a pool of sera IgE taken from a group of at least two individuals that are allergic to the unmodified food allergen.

40. **(Previously presented)** The nucleotide molecule of claim 37 wherein at least one modified amino acid is located in the center of the at least one IgE epitope.

41. **(Previously presented)** The nucleotide molecule of claim 37 wherein at least one amino acid in the at least one IgE epitope of the unmodified food allergen has been modified by substitution.

42. **(Previously presented)** The nucleotide molecule of claim 41 wherein at least one hydrophobic amino acid in the at least one IgE epitope of the unmodified food allergen has been substituted by a neutral or hydrophilic amino acid.

43. **(Previously presented)** The nucleotide molecule of claim 37 wherein the modified food allergen activates T cells.

44. **(Previously presented)** The nucleotide molecule of claim 37 in a vector for expression in a host cell.

45. **(Previously presented)** The nucleotide molecule of claim 37 wherein the modified food allergen is based on a protein obtained from a source selected from the group consisting of legumes, milks, grains, eggs, fish, crustaceans, and mollusks.

46. **(Previously presented)** The nucleotide molecule of claim 45 wherein the modified food allergen is based on a protein obtained from a source selected from the group consisting of wheat, barley, cow milk, egg, codfish, hazel nut, soybean, and shrimp.

47-55. **(Canceled)**

56. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-6 amino acid residues have been modified in the at least one IgE epitope.

57. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-5 amino acid residues have been modified in the at least one IgE epitope.

58. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-4 amino acid residues have been modified in the at least one IgE epitope.

59. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-3 amino acid residues have been modified in the at least one IgE epitope.

60. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-2 amino acid residues have been modified in the at least one IgE epitope.

61. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1 amino acid residue has been modified in the at least one IgE epitope.

62-67. **(Canceled)**

Attachment II

to

Appeal Brief under 37 C.F.R. § 1.192

Pending Claims after Entrance of Amendment

Pending Claims after Entrance of Amendment

1-36. **(Canceled)**

37. **(Previously presented)** A nucleotide molecule encoding a modified food allergen whose amino acid sequence is substantially identical to that of an unmodified food allergen except that at least one amino acid has been modified in at least one IgE epitope so that IgE binding to the modified food allergen is reduced as compared with IgE binding to the unmodified food allergen, the at least one IgE epitope being one that is recognized when the unmodified food allergen is contacted with serum IgE from an individual that is allergic to the unmodified food allergen.

38. **(Previously presented)** The nucleotide molecule of claim 37 wherein at least one amino acid has been modified in all the IgE epitopes of the unmodified food allergen.

39. **(Previously presented)** The nucleotide molecule of claim 37 wherein the at least one IgE epitope is one that is recognized when the unmodified food allergen is contacted with a pool of sera IgE taken from a group of at least two individuals that are allergic to the unmodified food allergen.

40. **(Previously presented)** The nucleotide molecule of claim 37 wherein at least one modified amino acid is located in the center of the at least one IgE epitope.

41. **(Previously presented)** The nucleotide molecule of claim 37 wherein at least one amino acid in the at least one IgE epitope of the unmodified food allergen has been modified by substitution.

42. **(Currently amended)** The nucleotide molecule of claim 41 wherein at least one amino acid in the at least one IgE epitope of the unmodified food allergen is hydrophobic, and wherein said at least one hydrophobic amino acid has been substituted by a neutral or hydrophilic amino acid.

43. **(Previously presented)** The nucleotide molecule of claim 37 wherein the modified food allergen activates T cells.

44. **(Previously presented)** The nucleotide molecule of claim 37 in a vector for expression in a host cell.

45. **(Previously presented)** The nucleotide molecule of claim 37 wherein the modified food allergen is based on a protein obtained from a source selected from the group consisting of legumes, milks, grains, eggs, fish, crustaceans, and mollusks.

46. **(Previously presented)** The nucleotide molecule of claim 45 wherein the modified food allergen is based on a protein obtained from a source selected from the group consisting of wheat, barley, cow milk, egg, codfish, hazel nut, soybean, and shrimp.

47-55. **(Canceled)**

56. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-6 amino acid residues have been modified in the at least one IgE epitope.

57. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-5 amino acid residues have been modified in the at least one IgE epitope.

58. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-4 amino acid residues have been modified in the at least one IgE epitope.

59. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-3 amino acid residues have been modified in the at least one IgE epitope.

60. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1-2 amino acid residues have been modified in the at least one IgE epitope.

61. **(Previously presented)** The nucleotide molecule of claim 37, wherein 1 amino acid residue has been modified in the at least one IgE epitope.

62-67. **(Canceled)**

Attachment III

to

Appeal Brief under 37 C.F.R. § 1.192

Food allergens listed in the "Official list of allergens" maintained by the IUIS Allergen Nomenclature Subcommittee

printed on June 8, 2003 from ftp://biobase.dk/pub/who-iuis/allergen.list

Official list of allergens
IUIS Allergen Nomenclature Subcommittee
ftp://biobase.dk/pub/who-iuis/allergen.list

2000.03.01 Jorgen Nedergaard Larsen and Henning Lowenstein,
ALK-Abello, Boge Alle 6-8, DK-2970 Horsholm, Denmark
Please report changes, additions or comments to jnlarsen@inet.uni2.dk

Legends: MW determined by reducing SDS-PAGE; asterisk: MW deduced from sequence;
C: cDNA seq; P: peptide seq;

Allergen source	Systematic and original names	MW kDa	sequence data	Accession # or References
Gadus callarias (cod)	Gad c 1; allergen M	12	C	112,113
Salmo salar (Atlantic salmon)	Sal s 1; parvalbumin	12	C	X97824 X97825
Bos domesticus (domestic cattle) (milk) (see also animals)	Bos d 4; alpha-lactalbumin	14.2	C	M18780
	Bos d 5; beta-lactoglobulin	18.3	C	X14712
	Bos d 6; serum albumin	67	C	M73993
	Bos d 7; immunoglobulin	160		77
	Bos d 8; caseins	20-30		77
Gallus domesticus (chicken)	Gal d 1; ovomucoid	28	C	114,115
	Gal d 2; ovalbumin	44	C	114,115
	Gal d 3; conalbumin (Ag22)	78	C	114,115
	Gal d 4; lysozyme	14	C	114,115
	Gal d 5; serum albumin	69	C	X60688
Metapenaeus ensis (shrimp)	Met e 1; tropomyosin		C	U08008
Penaeus aztecus (shrimp)	Pen a 1; tropomyosin	36	P	116
Penaeus indicus (shrimp)	Pen i 1; tropomyosin	34	C	117
Todarodes pacificus (squid)	Tod p 1; tropomyosin	38	P	117A
Haliotis Midae (abalone)	Hal m 1	49	-	117B
Apium graveolens (celery)	Api g 1; Bet v 1 homologue	16*	C	Z48967 AF129423
	Api g 4; profilin	55/58	P	P81943
	Api g 5;			

Brassica juncea (oriental mustard)	Bra j 1; 2S albumin	14	C	118
Brassica rapa (turnip)	Bra r 2; prohevein-like protein	25	?	P81729
Hordeum vulgare (barley)	Hor v 15; BMAI-1	15	C	119
Zea mays (maize, corn)	Zea m 14; lipid transfer prot.	9	P	P19656
Oryza sativa (rice)	Ory s 1;		C	U31771
Corylus avellana (hazelnut)	Cor a 1.0401; Bet v 1 homologue	17	C	AF136945
Malus domestica (apple)	Mal d 1; Bet v 1 homologue		C	X83672
	Mal d 2; thaumatin homologue		C	AJ243427
	Mal d 3; lipid transfer protein	9	C	Pastorello
Pyrus communis (pear)	Pyr c 1; Bet v 1 homologue	18	C	AF05730
	Pyr c 4; profilin	14	C	AF129424
	Pyr c 5; isoflavone reductase homologue	33.5	C	AF071477
Persea americana (avocado)	Pers a 1; endochitinase	32	C	Z78202
Prunus armeniaca (apricot)	Pru ar 1; Bet v 1 homologue		C	U93165
	Pru ar 3; lipid transfer protein	9	P	
Prunus avium (sweet cherry)	Pru av 1; Bet v 1 homologue		C	U66076
	Pru av 2; thaumatin homologue		C	U32440
	Pru av 4; profilin	15	C	AF129425
Prunus persica (peach)	Pru p 3;lipid transfer protein	10	P	P81402
Sinapis alba (yellow mustard)	Sin a 1; 2S albumin	14	C	120
Glycine max (soybean)	Gly m 1.0101; HPS	7.5	P	121
	Gly m 1.0102; HPS	7	P	121
	Gly m 2	8	P	A57106
	Gly m 3; profilin	14	C	AJ223982
Arachis hypogaea (Peanut)	Ara h 1; vicilin	63.5	C	L34402
	Ara h 2; conglutin	17	C	L77197
	Ara h 3; glycinin	60	C	AF093541

	Ara h 4; glycinin	37	C	AF086821
	Ara h 5; profilin	15	C	AF059616
	Ara h 6; conglutin homolog	15	C	AF092846
	Ara h 7; conglutin homolog	15	C	AF091737
Actinidia chinensis (kiwi)	Act c 1; cysteine protease	30	P	P00785
Solanum tuberosum (potato)	Sola t 1; patatin	43	P	P15476
Bertholletia excelsa (Brazil nut) P04403,M17146	Ber e 1; 2S albumin	9	C	
Juglans regia (English walnut)	Jug r 1; 2S albumin		C	U66866
	Jug r 2; vicilin	44	C	AF066055
Ricinus communis (Castor bean)	Ric c 1; 2S albumin		C	P01089

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